

Diabetes Mellitus and Hypoparathyroidism in a Girl with Mitochondrial Disease



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BACKGROUND

Mitochondrial disease can cause several endocrine disorders. Diabetes mellitus is the most common endocrine problem in mitochondrial disease. However mitochondrial disease is a rare cause for DM in children and adolescents. Other endocrine problems can also associate with DM in mitochondrial diseases. DM together with hypoparathyroidism have not been reported in childhood before. Here we report a 13 year old female patient presenting with DM, hypoparathyroidism, deafness, external ophthalmoplegia, ptosis, short stature and myopathy.

CASE REPORT

A 13-year-old girl was admitted to our clinic for blood glucose regulation. Her medical history revealed that she was diagnosed with type 1 diabetes mellitus at 11 years due to high blood glucose level. Simultaneous C-peptide and insulin levels were very low, however anti-GAD, anti-islet cell and anti-insulin antibodies were negative. (Table 1)

Table 1. Laboratory data at 11 years

Glucose	Urine Analysis	Venous pH Bicarbonate	Insulin	C peptide	HbA1c	Anti GAD Anti İnsülin İslet Cell Ab.
302 mg/dl	Ketone+ Glucose +++	7.4 24.9	3.2 µU/ml (4-25)	0.92 ng/ml (0.9-7.1)	10.2	Negative

Insulin was started, however frequent hypoglycemic episodes required replacing insulin with diabetic diet alone. HbA1c decreased to 5.4% on diabetic diet.

At 12 years she developed paresthesias of the hands and perioral numbness during illness. Laboratory data determined at 12 years is shown in Table 2.

Table 2. Laboratory data at 12 years

Ca	P	ALP	PTH
8.4 mg/dl (8.8-10.6)	6.8 mg/dl (4.5-5.5)	239 U/L (51-362)	10.6 pg/ml (15-68.3)

She was diagnosed with hypoparathyroidism. Low dose calcitriol treatment was started.

At 13 years of age, she was referred to us for blood glucose regulation and insulin had to be reintroduced due to an increase in HbA1c to 8.4%. She was the second child of unrelated parents. Her grandmother had type 2 diabetes and a maternal aunt had ptosis.



Physical Examination:

Height :133.5 cm (<3p)

Weight: 47 kg (<3p)

BMI: 12.2 kg/m² (<3p)

- Hypertrichosis
- Pectus excavatum
- Tanner stage 3 puberty
- External ophthalmoplegia
- Bilateral ptosis

Table 3. Laboratory data in our clinic

Fasting Glucose	Postprandial glucose	Fasting insulin	Postprandial insulin	C peptide
105 mg/dL	178 mg/dL	3.7 µU/ml	9.7 µU/mL	0.79 ng/mL (0.9-7.1)

Endocrinopathies presenting in association with external ophthalmoplegia, ptosis suggested mitochondrial disease. So we analyzed her for findings of mitochondrial disease.

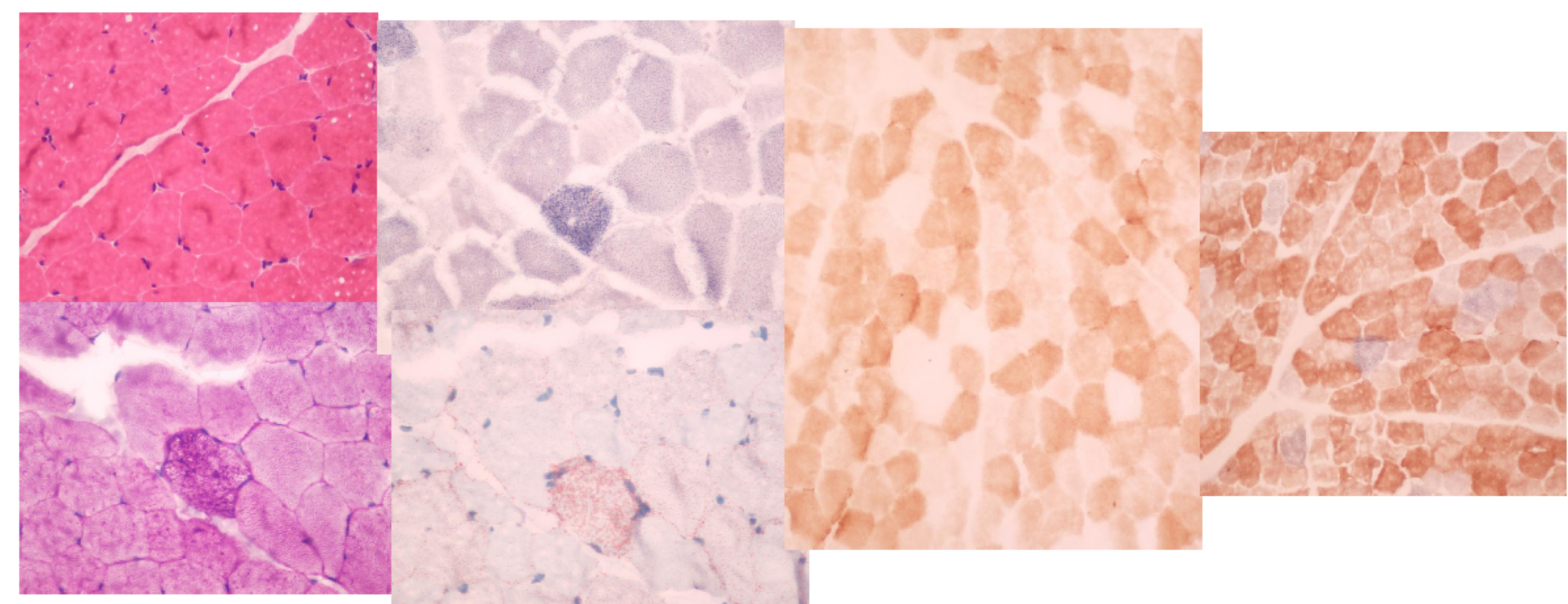
Lactic acid: **39.3 mg/dL (4.5-19.8)**

Pyruvic acid: **1.04 mg/dL (0.3-0.9)**

Audiometric studies: **Complete sensorineural hearing loss at high frequencies**

Echocardiography: Mild mitral valve regurgitation

Muscle biopsy: **Ragged -blue fibers and cytochrome c oxidase negative fibers compatible with mitochondrial myopathy.**



Results of the tests regarding mitochondrial disease indicate a mitochondrial disease. Mitochondrial DNA were studied in blood leukocytes and muscle tissue. Polymerase chain reaction was used to screen for mutations. First result indicated that she didn't have a A to G transition at nucleotide position 3243 in mitochondrial DNA. For elucidating the genetic reason studies are continuing.

She is currently on rapid acting insulin analogs solely before meals. The last HbA1c was 7.1 %.

CONCLUSIONS

Diabetes due to mitochondrial mutations and deletions is rare in the pediatric age group. Although hypoparathyroidism has also been described in mitochondrial disease, there have been few molecular studies in children. Coexistence of these two endocrinopathies in a child with mitochondrial disease is extremely rare .

Diabetes mellitus accompanying hypoparathyroidism, is an expected finding in autoimmune polyglandular syndrome. This patient reminds that it may also be seen in mitochondrial disease, however rare. Thus one should consider mitochondrial disease in the differential diagnosis of patients with multiple endocrine abnormalities even when weakness or myopathy is absent. Also complete endocrine evaluation should be part of mitochondrial disease.